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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,443	05/18/2005	Bertrand Saunier	NIH341.001NP	4458
45311 7590 08/29/2008 KNOBBE, MARTENS, OLSON & BEAR, LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614				
EXAMINER BOESEN, AGNIESZKA				
ART UNIT 1648		PAPER NUMBER		
MAIL DATE 08/29/2008		DELIVERY MODE PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/524,443

**Applicant(s)**

SAUNIER ET AL.

**Examiner**

AGNIESZKA BOESEN

**Art Unit**

1648

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 2, 5, 6, 9, 10, 12 and 13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5, 6, 9, 10, 12 and 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

The Amendment filed May 8, 2008 in response to the Office Action of January 8, 2008 is acknowledged and has been entered. Claims 1, 5 and 9 have been amended; claims 3 and 11 have been canceled. Claims 1-3, 5, 6, 9, 10, 12 and 13 are pending and under examination. The rejection of canceled claims 3 and 11 is moot.

#### ***Claim Rejections - 35 USC § 103***

Rejection of claims 1, 2, 5, 6, 9, 10, 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Lewis (US Patent 5,521,082) in view of Houghton (US Patent 5,350,671) and Baumert et al. (Journal of Virology, May 1998, IDS of 7/3/2006) **is withdrawn**.

However in view of Applicant's amendment a new rejection is made using the prior art references cited in the withdrawn rejection and new references teaching the newly amended limitation.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**Claims 1, 2, 5, 6, 9, 10, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis (US Patent 5,521,082) in view of Houghton (US Patent 5,350,671), Baumert et al. (Journal of Virology, May 1998, IDS of 7/3/2006), Revilla et al. (The Journal of Biological Chemistry, 1998, Vol. 273, p. 5405-5411) and Kwon (US Patent 6,974,863 B2).**

Applicants amended the claims to incorporate the limitation from claim 3 and to include a negative limitation "wherein the cells are lysed without sonication". Applicants note that while Baumert et al. teach using digitonin to lyse the cells, Baumert additionally uses sonication. Applicants argue that the cited references provide no reason to omit the step of sonication. In response to Applicant's arguments the Office cites new references which provide motivation to omit the step of sonication.

Revilla et al. teach isolating CMV viral particles from cells by lysing the cells by incubating the cells with protease inhibitors and 1% digitonin (see page 5406, Immunoprecipitation). Revilla et al. does not teach sonication being required for lysis and isolation of viral particles from the cells. Kwon teach lysing insect cells comprising baculovirus encoded proteins by incubating the cells in 1% digitonin lysis buffer (see column 38, lines 50-65 and column 40, lines 31-45). Kwon does not teach sonication being required for lysis of insect cells. Thus because the prior art teaches that digitonin at the concentration of less than 0.25 % is successfully used to lyse the cells and release viral particles, the skilled artisan would have been motivated to omit the step of sonication as presently required by the claims.

It would have been obvious to those skilled in the art to provide a method comprising lysing the cells infected with baculovirus expressing HCV structural proteins by incubating the cells in a buffer comprising protease inhibitors and less or equal to 0.25% digitonin and without the step of sonication, because Revilla and Kwon teach that using 1% digitonin lysis buffer successfully lyses the cells.

One would have been motivated to omit the step of sonication because the function of sonication is not required for the lysis of cells as evidenced by Revilla and Kwon. See MPEP

Art Unit: 1648

2144.04. Omission of an Element and Its Function Is Obvious if the Function of the Element Is Not Desired. Both Revilla and Kwon provide evidence that omission of the sonication step and using 1% digitonin lysis buffer is sufficient to lyse the cells. Thus omission of sonication step would have been obvious at the time of the present invention.

One would have had a reasonable expectation of success to isolate the infection defective HCV structural proteins from cells infected with baculovirus encoding and expressing HCV structural proteins by lysing the cells by incubating the cells with protease inhibitors and less or equal to 0.25% digitonin and without the step of sonication, because Revilla and Kwon teach that using 1% digitonin lysis buffer is sufficient to lyse the cells.

The teachings of Lewis, Houghton and Baumert discussed in the Office action of January 8, 2008 are reiterated below:

Lewis teaches a method of isolating infection defective hepatitis A virus (HAV) structural proteins from cells infected with HAV, comprising lysing the infected cells by incubating the cells in hypotonic buffer, adding polyethylene glycol to the lysate to form a precipitate and fractionating the precipitate by gradient ultracentrifugation (see the entire document, particularly the figure on the face of the Patent, claims 1-6, and column 6, lines 5-29). Lewis does not expressly teach that his method can be used to purify infection defective HCV structural protein complexes from cells infected with a baculovirus encoding and expressing HCV structural proteins. Lewis does not teach lysing the cells in a buffer containing digitonin and protease inhibitors.

Houghton teaches isolation of HCV particles from cell cultures by precipitation with polyethylene glycol (see column 40, lines 31-41). Houghton does not teach the lysis step of the

Art Unit: 1648

present method. Houghton teaches baculovirus expression system for expression of viral genomes (see column 47, lines 20-26). Baumert et al. teach isolation of two VLP constructs: E1 and E2-p7, and another VLP construct comprising E1 and E2 without p7 proteins, particles are 50 nm in diameter (see Figure 1, Figure 4 and Materials and Methods –Baculovirus constructs and insects cell cultures, and page 3831). Baumert teaches lysing the cells in a buffer containing digitonin and protease inhibitors (see Materials and Methods). Baumert teaches centrifuging the cell lysate through a cushion comprising sucrose, a disaccharide (see Materials and Methods - Purification of HCV-like particles, and page 3831). Baumert provides evidence that the HCV structural proteins have been successfully expressed using baculovirus expression system.

It would have been obvious to those skilled in the art to provide a method comprising lysing the cells infected with baculovirus expressing HCV structural proteins and to precipitate the HCV viral proteins from the cell lysate with polyethylene glycol. One would have been motivated to use Lewis' method to isolate Baumert's infection defective HCV structural proteins because Houghton expressly suggests that HCV particles can be precipitated from cell cultures with polyethylene glycol. One would have been motivated to treat the cells with hypertonic and hypotonic shock for the purpose of lysing the cells and to adjust the concentration of digitonin to less than or equal to 0.25%. Adjusting the concentration of digitonin is merely routine optimization of lysing conditions.

One would have had a reasonable expectation of success to isolate the infection defective HCV structural proteins from cells infected with baculovirus encoding and expressing HCV structural proteins by precipitation with polyethylene glycol, because polyethylene glycol has

been known and used in the art for the precipitation and isolation of viral proteins from virus infected cells as evidenced by Lewis and Houghton.

Therefore the claims would have been *prima facie* obvious to the skilled artisan at the time when the invention was made.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground of rejections presented in this Office action. Thus, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/  
Examiner, Art Unit 1648

/Bruce Campell/  
Supervisory Patent Examiner, Art Unit 1648